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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/083,682 | 10/24/2001 | Alan P. Wolffe | 8325-0015.20 | 1541 |

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| EXAMINER | |
|---|---|
| ZHOU, SHUBO | |
| ART UNIT | PAPER NUMBER |
| 1631 | |

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/083,682 | WOLFFE ET AL. | |
| | Examiner | Art Unit | |
| | Shubo (Joe) Zhou | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *66-71 and 125-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-71 and 125-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



HC

## DETAILED ACTION

1. Applicants' amendments and request for reconsideration in the communication filed on 12/10/04 are acknowledged and the amendments entered.

2. Applicant's arguments in response to the previous Office action have been fully considered but they are not deemed to be persuasive. The following rejections and/or objections are reiterated from the previous Office action, mailed 9/9/04, and constitute the complete set presently being applied to the instant application. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

3. The rejection of claims 16-20 under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement, is hereby withdrawn in view of applicants' amendments to the claims, wherein claims 16-20 are canceled.

4. The rejection of claims 1-6, 8-15, and 21-26 under 35 U.S.C. 112, first paragraph, wherein the claims are rejected because the specification, while being enabling for practicing the claimed method involving using a probe to mark the chromatin with any marks but methylation, or when marking the chromatin with methylation, digesting the methylated chromatin with a methylation-sensitive restriction enzyme and isolating the methylation-marked fragments, does not reasonably provide enablement for practicing the method involving methylating the chromatin, digesting the methylated chromatin with a methylation-dependent restriction enzyme, is hereby withdrawn in view of applicants' amendments to the claims, wherein claims 1-6, 8-15, and 21-26 are canceled.

5. The rejection of claims 66-71 are under 35 U.S.C. 112 , second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is hereby withdrawn upon reconsideration and in view of applicants' amendments to the claims.

6. The rejection of claims 1-2, 4-9, 13-19, 21-25 under 35 U.S.C. 103(a) as being obvious over van Steensel et al. (Nature Biotechnology, Vol. 18, pages 424-428, April 2000, journal received by the STIC of the USPTO on 4/19/2000) in view of Bringmann et al. (FEBS Letters, Vol. 213, number 2, pages 309-315, 1987), is hereby withdrawn in view of applicants' amendments to the claims, wherein these claims are canceled.

7. The rejection of claim 3 under 35 U.S.C. 103(a) as being obvious over van Steensel et al. (Nature Biotechnology, Vol. 18, pages 424-428, April 2000, journal received by the STIC of the USPTO on 4/19/2000) in view of Bringmann et al. (FEBS Letters, Vol. 213, number 2, pages 309-315, 1987), as applied to claims 1-2, 4-9, 13-19, 21-25 above, further in view of Grosveld et al. (US patent 5,635,355, Jun 3, 1997), is hereby withdrawn in view of applicants' amendments to the claims, wherein the claim is canceled.

8. The rejection of claims 12, 20 and 26 under 35 U.S.C. 103(a) as being obvious over van Steensel et al. (Nature Biotechnology, Vol. 18, pages 424-428, April 2000, journal received by the STIC of the USPTO on 4/19/2000) in view of Bringmann et al. (FEBS Letters, Vol. 213, number 2, pages 309-315, 1987), as applied to claims 1-2, 4-9, 13-19, 21-25 above, further in view of Gross (Ann. Rev. Biochem., 1988, 57:159-197), is hereby withdrawn in view of applicants' amendments to the claims, wherein these claims are canceled.

9. The rejection of claims 1-4, 10-11, and 13-15 under 35 U.S.C. 103(a) as being obvious over Grosveld et al. (US patent 5,635,355, Jun 3, 1997) in view of Tanguay et al. (Nucleic Acids

Research, Vol. 18, page 5902, 1990), is hereby withdrawn in view of applicants' amendments to the claims, wherein these claims are canceled.

10. The rejection of claim 12 under 35 U.S.C. 103(a) as being obvious over Grosveld et al. (US patent 5,635,355, Jun 3, 1997) in view of Tanguay et al. (Nucleic Acids Research, Vol. 18, page 5902, 1990), as applied to claims 1-4, 10-11, and 13-15 above, further in view of Gross (Ann. Rev. Biochem., 1988, 57:159-197), is hereby withdrawn in view of applicants' amendments to the claims, wherein the claim is canceled.

11. The provisional rejection of claims 1-4, and 10-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 123-142, and 147-152 of US copending Application No. 09/844,501 (US App. Pub. No. 20020081603), is hereby withdrawn in view of applicants' amendments to the claims, wherein these claims are canceled.

12. The provisional rejection of claims 5-9, and 16-26 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 123-124, 128-130, 134-143, 145-147, and 151-152 of copending Application No. 09/844,501, is hereby withdrawn in view of applicants' amendments to the claims, wherein these claims are canceled.

***Correction of Inventorship***

13. Applicants' request for change of inventorship pursuant to 37 CFR 1,48(b) is acknowledged, and the inventorship for this application has been changed accordingly.

***Declaration***

14. The supplemental declaration filed 12/10/04, wherein it is signed by the administrator, Elizabeth Wolffe, of the deceased inventor Alan Wolffe, is acknowledged and accepted.

***Claim Rejections-35 USC § 112***

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 66-71 and newly added claims 125-128 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a polynucleotide or a library of polynucleotides comprising polynucleotides corresponding to the accessible regions of cellular chromatin. Each of these claims is directed to a genus comprising any library of polynucleotides comprising polynucleotides corresponding to the accessible regions of cellular chromatin obtained by the method of the claim. Further, since the probes used in the claims may be a chemical, an enzyme or an antibody, each of which may react with, and thus mark, different polynucleotides, the claimed genus comprises different species of libraries comprising different polynucleotides.

A description of a genus may be achieved by means of a recitation of a representative number of species, falling within the scope of the genus, or by means of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case, however, the specification does not describe the structure (i.e. the sequences of each clone of a library) of any species, nor does it describe any structural feature (i.e. the sequence of each clone in a library) common to the members of the genus. No common structural attributes identify the members of the genus. While the specification gives example of how to make a library (see pages 113-116), it does not describe the structure of the library or libraries made. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common structural attributes or characteristics that identify members of the genus, and because the genus is highly variable, the mere example of a method to make a library is insufficient to describe the genus. One of skill in the art would reasonably conclude that applicant was not in possession of the claimed genus at the time the application was filed.

The rejection is reiterated from the previous Office action.

Applicants' arguments filed 12/10/04 have been fully considered but they are not persuasive.

Applicants' argument is on the ground that there is requirement for the applicant to describe the structure of each of the species of the genus, but the specification only needs to convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

applicant was in possession of the invention as now claimed, and that in the instant case, the specification does contain representative examples of possible library clones, namely SEQ ID N0s: 10, 11 and 12.

This is not found persuasive because, firstly, applicants do not provide evidence or arguments as to how the specification of the instant application convey with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. In the contrary, as set forth above, since the structures of an accessible regions of chromatin vary considerably depending on what reagent the chromatin is accessible to. For example, the structure of a region of chromatin that is accessible to a methylase would be different from the structure of a region of chromatin that is accessible to an antibody that binds to DNase I. Further, as set forth above, while the specification gives example of how to make a library and provides examples of SEQ ID N0s: 10, 11 and 12, it does not describe the structure of the library or libraries made. For reasons given above, the sequences of SEQ ID N0s: 10, 11 and 12 would not be representative of the molecules of the claimed library. Thus, one of skill in the art would reasonably conclude that applicant was not in possession of the claimed genus at the time the application was filed.

### *Claim Rejections-35 USC § 102*

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 66-71 and newly added claims 125-128 are rejected under 35 U.S.C. 102(b) as being anticipated by Clontech (Clontech Catalog, 1998-1999, pages 177-183, Clontech Laboratories, Inc., Palo Alto, California).

The claims are drawn to a polynucleotide or a library comprising the polynucleotides. Each member of the library comprises an insert and a vector, and the insert sequence consists essentially of accessible regions of cellular chromatin.

The claims, as currently written, are apparently product-by-process claims.

The court in *In re Thorpe 777 F.2d 695, 698, 227 USPQ 964,966 (Fed. Cir. 1985)* holds:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Clontech Catalog discloses multiple genomic libraries made from different organisms with cellular chromatin using different vector systems. See pages 177-183, especially the table on pages 182-183. These genomic libraries are made by a method involving digesting the whole genomes of the chromatin of different organisms with Sau3A I or Mbo I, which are four cutters and are known to digest the genomes with high frequency, and cloning the digested fragments in different vector systems. See page 177. It would be readily apparent to one of skill in the art that the libraries produced by such a method inherently comprise clones that have an insert that either consists of polynucleotide from regions of cellular chromatin that are accessible to reagents such as nuclease and restriction enzymes, as recited in claims 125-128, and that such

libraries should comprise clones with an insert that comprises polynucleotides from the accessible region and the inaccessible region. The catalog discloses a plurality of libraries comprising polynucleotides from cellular chromatin of cells at a particular stage of the development, such as from mouse of ages of 9-11 weeks, and adult, and a plurality of libraries comprising polynucleotides from a particular tissue, such as mouse kidney and mouse liver. See the listing of genomic libraries on pages 182-183.The catalog also discloses a plurality of libraries comprising polynucleotides from healthy and diseased cells, such as normal muscle of Xenopus laevis and human Hela S3 cells (from ATCC#CCL2.2, see page 182), which are diseased (cancer) cells and infected with viruses. See page 1 of 3 of the printout of ATCC catalog from ATCC's website:
http://www.atcc.org/SearchCatalogs/longview.cfm?atccsearch=yes.

Applicants' arguments filed 12/10/04 have been fully considered but they are not persuasive.

Applicants' argument is on the ground that the methods used to generate the libraries as disclosed by Clontech are different from the methods used to generate the claimed library. Naked DNA is digested in the Clontech reference whereas chromatin is digested in the instant application. Therefore, the insert in the claimed library consists essentially of polynucleotide from the accessible region whereas the Clontech libraries also have insert that has polynucleotides from the inaccessible regions. This is not found persuasive for the following reasons:

With regard to the term "consisting essentially of", it is interpreted pursuant to the Office's policy as set forth in foot note number 29 of the "Guidelines for Examination of Patent

Applications Under the 35 U.S.C. 112, ¶ 1, 'Written Description' Requirement" (Federal Register/Vol. 66, No.4, Friday, January 5, 2001), which is copied below:

> *''By using the term 'consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a 'consisting of' format and fully open claims that are drafted in a 'comprising' format.'' PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353–54 (Fed. Cir. 1998). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to ''comprising.'' See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 (''PPG could have defined the scope of the phrase ''consisting essentially of'' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention.''). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895–96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of ''consisting essentially of,'' applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964).*

Accordingly, the insert of each clone in the claimed library is interpreted to comprise polynucleotides that correspond to the accessible region and inaccessible regions of the cellular chromatin. Thus, the claims read on the Clontech libraries, which inherently have clones with

inserts that are only from the accessible region, and clones with an insert that comprises polynucleotide from the accessible region and the inaccessible region.

***Conclusion***

19. No claim is allowed.

20. **THIS ACTION IS MADE FINAL.**

21. Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or

relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shubo (Joe) Zhou, Ph.D.

Patent Examiner

J. S. Brusca 21 March 2005

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER